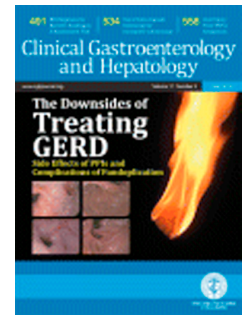


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Factor Analysis Defines Distinct Upper and Lower Gastrointestinal Symptom Groups Compatible With Rome IV Criteria in a Population-based Study

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MS has received unrestricted research grants from Danone and Ferring Pharmaceuticals, and served as a Consultant/ Advisory Board member for AstraZeneca, Danone, Nestlé, Menarini, Almirall, Allergan, Albireo, Glycom and Shire, and as a speaker for Tillotts, Takeda, Menarini, Allergan Shire and Almirall.

Author contributions:

All authors were involved in study concept and design, collecting/interpreting data, and drafting/revising the manuscript. All authors have approved the final draft submitted.

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Abstract

Background and aims: The Rome IV criteria define functional gastrointestinal (GI) disorders by specific combinations of symptoms. It is possible to empirically evaluate these symptom combinations by factor analysis (a statistical procedure that groups variables that correlate). However, this analysis has not been performed for the Rome IV criteria, and factor analyses based on the previous versions of the Rome criteria did not use population-based data. We therefore investigated symptom grouping by the Rome IV questionnaire using factor analysis of a population-based sample.

Methods: The Rome IV questionnaire was completed online in English by 5931 respondents from the United Kingdom, United States, and Canada (49% female, age range, 18–92 years). We performed an exploratory factor analysis on the Rome IV questions. Next, we performed a confirmatory factor analysis to compare the exploratory factor result to that of the Rome IV criteria.

Results: The exploratory factor analysis identified 8 factors that accounted for 45% of the variance in response: constipation, diarrhea, irritable bowel syndrome, abdominal pain, heartburn, nausea or vomiting, globus, and other upper GI symptoms. Most factors corresponded to distinct functional GI disorders defined by the Rome IV criteria—exceptions included abdominal pain and upper GI symptoms. In confirmatory factor analysis, the exploratory model fitted slightly better than that based on the Rome IV criteria (root mean square error of approximation, 0.063 vs 0.077).

Conclusion: We used factor analysis to identify distinct upper and lower GI symptom groups that are compatible with the Rome IV criteria. Our findings support the use of the Rome IV criteria in research and clinical practice as a basis for development of diagnostics and management of patients.

Keywords: IBS; FGID; validation; internet survey

Introduction

Functional gastrointestinal (GI) disorders (FGIDs) are syndromes defined by clusters of symptoms emanating from the GI tract, with population prevalences for many of these disorders ranging between 5 and 10%.¹ More than 20 FGIDs are defined by the published Rome IV criteria,² based on specific GI symptom combinations.

The distinction of each FGID as a separate entity may be corroborated by investigating how GI symptoms group together in the general population, and whether these symptom groupings are compatible with the Rome criteria. One method of doing so is factor analysis: a statistical procedure that groups variables with strong inter-correlations. Consistent agreement between factor analysis and the Rome symptom criteria would then suggest that the disorders represent distinct entities which are identified by these symptom criteria. Previous studies have performed factor analyses on GI symptoms, and compared the resulting factors to the structures of the Rome I and II criteria,^{3,4} as well as the Manning criteria for irritable bowel syndrome (IBS).⁵ For example, Whitehead *et al*⁶ found factors of IBS (i.e. abdominal pain related to stool patterns), nausea, constipation (including straining and incomplete evacuation), and a heterogeneous group of other GI symptoms. A similar IBS factor was found by Taub *et al*⁷ and Talley *et al*.⁸ Whitehead *et al*⁹ performed a factor analysis on GI symptoms in gastroenterology clinic patients, and reported thirteen distinct factors, including IBS, constipation, diarrhoea, and anorectal pain, but also several upper GI factors. Finally, Siah *et al*¹⁰ described amongst others a factor of bloating, associated with flatulence and belching. In conclusion, factor analyses can be used to substantiate the definitions of FGIDs.

The above factor analyses assessed Rome I, II, and III diagnostic classifications, but such analyses have not been performed since the publication of Rome IV. Furthermore, most of the previous factor analyses did not use population-based samples. We therefore aimed to empirically substantiate the latest definitions of FGIDs in a large, population-based sample by factor analysis.

Methods

Rome IV survey

We used an internet-based Rome IV survey involving 6300 individuals, with methodology described previously.¹ Briefly, participants were a nationally representative adult population sample from the United States (US), United Kingdom (UK), and Canada, as selected by the survey vendor Qualtrics Inc. Quota-based sampling was used to ensure equal proportion of sex (50:50), age groups (40% aged 18-39, 40% aged 40-64, and 20% aged 65 and older), and education level (30% maximum with more than sixteen years of formal education) across the countries. In the US sample, the survey vendor also selected 20% African Americans and 20% Hispanic ethnicity respondents, but these demographic shifts were not done in the UK or Canada. The survey was presented as a health survey without specific mention of gastroenterology, in order to prevent enrichment of participants with GI problems. All respondents confirmed informed consent online at the start of the survey. To ensure reporting quality, three questions were presented twice, and there were two attention verification questions. The survey was completed by a total of 6300 respondents, i.e. 2100 for the US, UK, and Canada respectively. Before data collection started, the study was reviewed by the Institutional Review Board (IRB) at the University of North Carolina and deemed IRB-exempt as all study participants were anonymous to the investigators.

Data pre-processing

Of the 6300 respondents, we included those who satisfied both attention verification questions and the response consistency checks with the three repeated symptom questions. This left 5931 respondents in the analysis sample. Of the 86 Rome IV questions, we included those with ordinal response scales, as these can be used to compute correlations. Excluded questions mostly related to the length of time the symptom had been present. No questions critical to a Rome IV FGID diagnosis were excluded. A total of 49 Rome IV questions were included in the analysis.

Exploratory factor analysis

We performed an exploratory factor analysis using the "factanal" function in R version 3.3.3.¹¹ This is a statistical procedure that groups variables with strong inter-correlations, and as such identifies the key variable groupings. A correlation matrix of the Rome IV questions was computed, and orthogonal factors with an eigenvalue larger than 1 were retained. Factor analysis was performed with maximum likelihood estimation and varimax rotation. Loadings of 0.40 and larger were deemed relevant.

Confirmatory factor analysis

We used confirmatory factor analysis to confirm that Rome IV successfully captures the GI symptoms into distinct FGID entities. This is done by fitting a pre-specified model of the Rome IV structure, and comparing this model to the data-driven structure resulting from the exploratory factor analysis. In case the models are similar of composition and statistical fit, this further reinforces the Rome IV criteria.

The factor structure of the Rome IV criteria was pre-specified as follows (see table 1 for reference). Globus was defined as a lump in the throat occurring between meals (items 1 and 3). Functional heartburn was defined by burning sensations in the chest (items 7 and 9). Functional dysphagia was defined by foods sticking in the oesophagus¹² (items 8 and 12). Postprandial distress syndrome was defined by postprandial fullness and early satiety (items 14 and 16). Chronic nausea and vomiting syndrome was defined by nausea and vomiting¹³ (items 21 and 23). IBS was defined by pain anywhere in the abdomen related to defecation (items 40, 41, 42, and 43). Functional constipation was defined by stools that are hard, infrequent, and hard to pass¹⁴ (items 49, 51, 52, 53, 54, and 55). Biliary pain was defined by pain in the right upper quadrant¹⁵ (items 68, 69, 70, 71, and 72). Other FGIDs were defined by only one eligible Rome IV question, and were not in the confirmatory model in order to be consistent with the exploratory model. The exploratory and Rome IV based models were compared by root mean square error of approximation (RMSEA).

Results

There were 5931 respondents in the analysis sample. The demographics approximated those from recent census reports¹⁶⁻¹⁸ by age and sex categories. The age ranged from 18 to 92 years old and 49% was female (figure 1). Common FGIDs were: functional dyspepsia, postprandial distress syndrome: 7.7%; functional constipation: 6.3%; proctalgia fugax: 5.9%; IBS: 5.7%; functional abdominal bloating/distension: 5.6%; functional diarrhoea: 5.4%.

Exploratory factor analysis

Eight distinct factors emerged from the factor analysis, and were characterised as constipation, diarrhoea, IBS, abdominal pain, heartburn, nausea/vomiting, globus, and other upper GI symptoms (table 1). Taken together, they explained 45% of the response variance. The constipation factor held all items that define functional constipation in Rome IV. Diarrhoea was described by loose stools, including those after a meal, as well as urgency, and was thus compatible with functional diarrhoea in Rome IV. The IBS factor held the Rome IV defining questions for IBS (abdominal pain related to defecation, stool frequency, and stool consistency) with large loadings ($r \geq 0.73$), but also pain in the epigastric or right upper quadrant regions related to defecation, albeit with smaller loadings ($r = 0.45$ and 0.48). In the factor of abdominal pain, pain was not associated with defecation but did interfere with usual activities, i.e. symptoms partially covering both biliary pain¹⁵ and centrally mediated abdominal pain syndrome in Rome IV.¹⁹ Heartburn and globus overlapped with the Rome IV definitions for functional heartburn and globus. The factor nausea/vomiting contained the items used to define chronic nausea and vomiting syndrome in Rome IV, plus retching and vomiting related to right upper quadrant pain ($r = 0.58$ and 0.63). Finally, there was a factor of upper GI symptoms, containing two symptoms of functional dyspepsia in Rome IV (epigastric pain and postprandial fullness), but also bloating, belching, abdominal pain, and some oesophageal symptoms. Some items stood in isolation, particularly pain with swallowing, early satiety, abdominal pain related to a meal, faecal incontinence, and anorectal pain ($r < 0.40$). All items and their rotated factor loadings are shown in table 1. Results separate for the three country samples are available in supplementary information (supplementary tables 1-3).

Of the 5931 respondents, 62% met the Rome IV symptom threshold for at least one single symptom that is part of the definition of FGIDs (figure 2). Symptoms were sometimes confined to one factor (19%), but often covered items from two (11%) or more (32%), indicating a degree of overlap between the various GI symptoms. The most common symptom was abdominal pain related to

defecation (21%) followed by bloating/abdominal distension and loose stools (19% each), whereas no oesophageal or gastroduodenal symptom was particularly common (maximum 10%).

As can be appreciated in figure 2, the IBS factor had the strongest within-factor loadings and correlations: of the 30% who met the Rome IV symptom threshold for at least one of the items in the IBS factor, 77% met the criteria for at least two items (note the contrasting black and white colour patterns for IBS in figure 2). By contrast, of the 33% who met the Rome IV symptom threshold for at least one upper GI item, only 51% met the criteria for at least two. Many upper GI items thus stood in isolation, possibly because many upper GI FGIDs are based on a single key symptom rather than a combination of symptoms, unlike most functional bowel disorders.

Confirmatory factor analysis

The exploratory factor model had a slightly better fit than that of the Rome IV model (RMSEA: 0.063 vs. 0.077, chi-square: 17500 vs. 8932, df: 712 vs. 247). However, the difference in fit was small, also given that the most factors and FGIDs were represented in both the exploratory and Rome IV model, with near-identical compositions (figure 3). As can be seen in figure 3, the confirmatory model had coefficients of a magnitude comparable to those of the exploratory model (these are the values on the diagonal lines: compare left versus right). One item had a negative coefficient in the confirmatory model: right upper quadrant pain at different intervals (item 71, -0.16, figure 3), indicating that it did not match well with the factor for biliary pain as hypothesised based on Rome IV.

Discussion

The present study empirically evaluated the symptom combinations in the Rome IV criteria, and found eight distinct symptom groupings, these being constipation, diarrhoea, IBS, abdominal pain, heartburn, nausea/vomiting, globus, and other upper GI symptoms. All in all these corresponded well with the Rome IV structure.²

The factors for IBS, constipation, diarrhoea, globus, heartburn, and nausea/vomiting closely matched the Rome IV criteria for IBS, functional constipation, functional diarrhoea,¹⁴ globus, functional heartburn,¹² and chronic nausea and vomiting syndrome¹³ respectively, thereby reinforcing the Rome IV criteria for these FGIDs. Moreover, these factors were quite similar to those reported in factor analyses of earlier Rome editions.⁶⁻¹⁰ The IBS factor was the most distinct, with respondents scoring either very high or very low on all defining questions. While constipation and diarrhoea are often seen in IBS patients, IBS is a heterogeneous condition, and as such it is not unexpected to see factors for the core element of IBS (pain related to stool patterns) as well as for the separate stool patterns.

We found a separate factor for abdominal pain, i.e. of a different nature than IBS, which also has been described in earlier studies.⁹ It covered both items from biliary pain (right upper quadrant pain)¹⁵ and centrally mediated abdominal pain syndrome (pain restricting usual activities).¹⁹ This factor does not cleanly represent biliary pain, as the item of the pain taking place at different intervals loaded negatively on this factor, while being a defining item in Rome IV. Instead it may represent centrally mediated abdominal pain syndrome, in which the pain is nearly continuously present. Nevertheless, it is difficult for respondents to sense exactly where the pain is located (possibly due to diffuse activation of nociceptive systems in visceral organs),²⁰ explaining the overlap between pains in the various abdominal sub-regions. Moreover, irrespective of factor structure, it is possible that symptoms overlap between different disorders due to common pathophysiological mechanisms.

Upper GI symptoms factored into heartburn, globus, and nausea/vomiting. There was also a factor with a combination of upper GI symptoms including functional dyspepsia and overlapping symptoms such as belching and bloating, which was also found by Siah *et al.*¹⁰ Whitehead *et al.*⁹ reported separate factors of heartburn, dysphagia, globus, rumination syndrome, and dyspepsia, capturing the structure proposed in Rome I. Others saw factors of nausea and gas/belching/acid^{6,7} or reflux.⁸ Factor analyses have also been performed on different questionnaires, such as the reflux disease questionnaire, where factors were found for regurgitation (e.g. acid taste), heartburn, and dyspepsia, although upper GI symptoms overlapped considerably,²¹ in line with the present study. Siah *et al.*¹⁰ further discussed a meal-related factor. Meal-related abdominal pain in the present study did not

load on any factor, with the largest loadings being for IBS ($r = 0.38$) and abdominal pain ($r = 0.33$). The existence of a broad factor of upper GI symptoms may imply a degree of common pathophysiology between these items. Common mechanisms may be peripheral or central. For example, Fischler *et al*²² found a factor of bloating and postprandial fullness to be associated with delayed gastric emptying, a factor of belching associated with gastric hypersensitivity, and a factor of epigastric pain associated with both gastric hypersensitivity and several psychosocial factors. In summary, the factor structure of upper GI symptoms found in the present study is quite consistent with those of prior studies, and partially reinforces the Rome IV criteria, although some upper GI symptoms were difficult to separate out using the Rome IV questionnaire.

Finally, confirmatory factor analysis showed that Rome IV groups symptoms in a manner that captures the variance in the population, close to the factors found through computerised means (i.e. the exploratory factor analysis). The item "right upper quadrant pain at different intervals", defining biliary pain in Rome IV, was the only odd one out to have a negative coefficient for this FGID. It may be considered to rephrase this item in future Rome editions.

Our study has two strengths. First, while factor analytical studies have contributed to amendments of Rome I, we present a factor analysis for the published Rome IV questionnaire. The results reinforce the Rome IV criteria, which can be used in research and clinical care for diagnostics and specific management of FGID patients. Second, we did so in a large sample in three countries, with demographics close to those of the general population. Generalisability of our findings to the population should therefore be high. It remains to be seen whether other languages, countries, or continents (e.g. Asia) would render similar findings,²³ although the recent factor analysis by Siah *et al*¹⁰ of Rome III shows that any differences are likely to be subtle. A limitation is the absence of information on how many potential respondents chose to ignore the invitation to partake in the survey, despite the close similarity between sample and population demographics. Furthermore, some FGIDs are described by only one key symptom in Rome IV, so that these will not be supported by factor analysis. However, it is useful to include these symptoms into the exploratory analysis to determine whether there are unpredicted symptom associations that should be recognised.

To conclude, upper and lower GI symptom groupings compatible with Rome IV diagnoses exist in the general population, and can be identified using the English Rome IV questionnaire in a large population-based sample from three English-speaking countries. Our results provide further basis for practising clinicians to use the Rome IV criteria throughout the process going from symptoms to diagnosis and management. While our results reinforce the Rome IV criteria, some upper GI symptoms were difficult to separate out, and more work is needed to reach a distinct classification.

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Figure captions

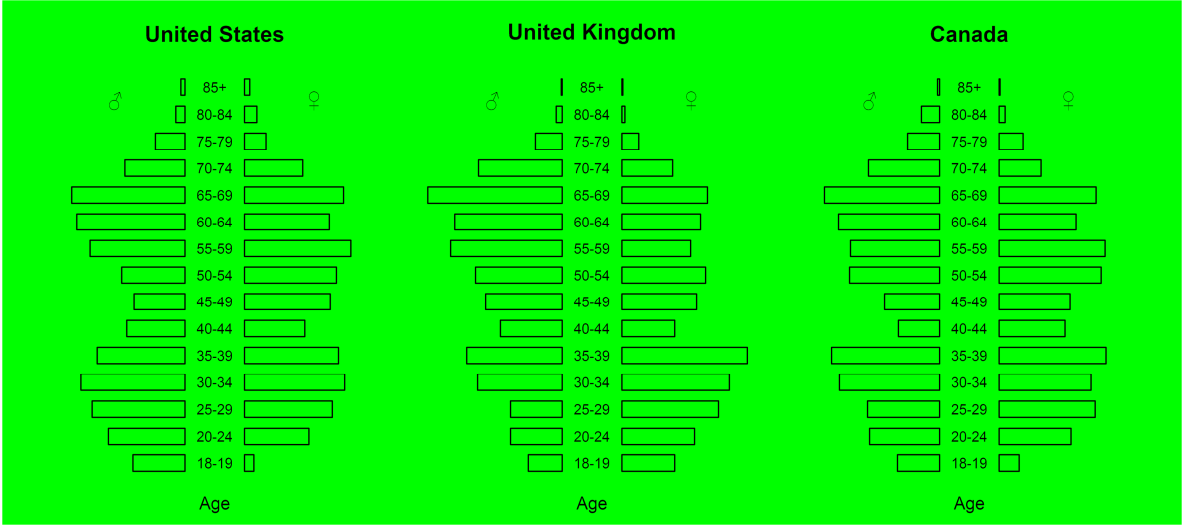
Figure 1: Age and sex of the respondents in the present study (bars) compared to those of recent census reports (shade).

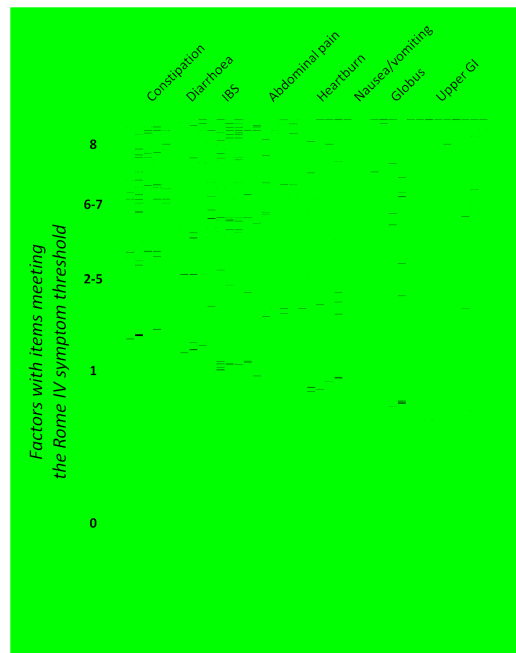
Figure 2: Raw data. Columns are Rome IV questions sorted numerically by factor. Rows are respondents, sorted by the number of factors with items meeting the Rome IV symptom threshold. Darker colours represent higher (worse) responses.

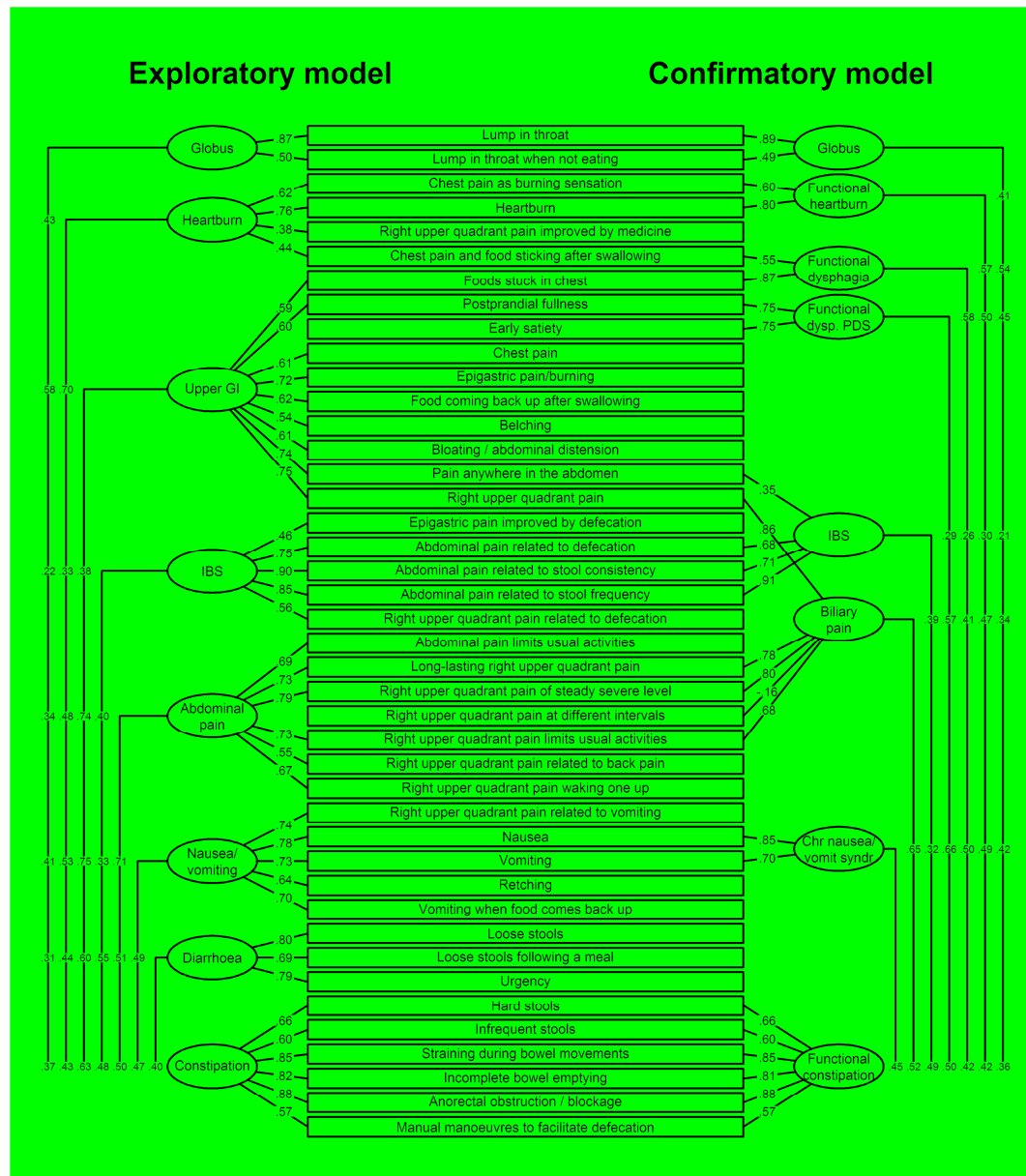
Figure 3: Schematic overview of the exploratory (left) and confirmatory (right) factor models. Ovals are factors, rectangles are Rome IV items. Values on diagonal lines are standardised coefficients (factor loadings), and indicate how strongly each item loads on the factor that it defines. Values on vertical lines denote covariances of factors. Values in boxes are error terms.

Table 1: Factor loadings after varimax rotation.

Item	Topic	Constipation	Upper GI	Abdominal pain	IBS	Nausea/vomiting	Diarrhoea	Heartburn	Globus
1	Lump in throat	.15	.36	.03	.02	.12	.08	.08	<u>.78</u>
3	Lump in throat when not eating	.09	.05	.19	.14	.08	.04	.19	<u>.48</u>
4	Pain with swallowing	.12	.17	.23	.08	.22	.03	.30	.07
5	Chest pain	.20	<u>.49</u>	.10	-.01	.18	.08	.22	.18
7	Chest pain as burning sensation	.07	.12	.19	.13	.05	.05	<u>.62</u>	.07
8	Chest pain and food sticking after swallowing	.09	.10	.08	.12	.18	.05	<u>.45</u>	.09
9	Heartburn	.15	<u>.41</u>	.07	.05	.11	.12	<u>.49</u>	.08
12	Foods stuck in chest	.18	<u>.43</u>	.05	.03	.20	.11	.33	.22
14	Postprandial fullness	.18	<u>.41</u>	.18	.04	.25	.13	.21	.08
16	Early satiety	.22	.36	.17	.05	.30	.13	.15	.09
18	Epigastric pain/burning	.15	<u>.55</u>	.29	.03	.25	.09	.26	.04
19	Epigastric pain/burning improved by defecation	.12	.03	-.05	<u>.45</u>	-.02	.00	.21	.10
21	Nausea	.16	.38	.29	.08	<u>.54</u>	.11	.11	.07
23	Vomiting	.11	.27	.15	.05	<u>.66</u>	.07	.10	.05
25	Self-induced vomiting	.06	.00	-.01	.00	.17	.09	.18	.07
32	Food coming back up after swallowing	.16	<u>.44</u>	.07	.08	.37	.12	.21	.12
34	Retching	.14	.14	.16	.07	<u>.58</u>	.14	.15	.09
35	Vomiting when food comes back up	.20	.15	.21	.09	<u>.63</u>	.13	.09	.01
37	Food coming back up is recognisable	.04	.10	.11	.12	.18	-.01	.05	.06
38	Belching	.09	<u>.40</u>	.15	.04	.27	.10	.19	.05
40	Pain anywhere in the abdomen	.25	<u>.63</u>	.33	.11	.13	.18	.02	.05
41	Abdominal pain related to defecation	.14	.03	.06	<u>.73</u>	-.01	.13	.03	.01
42	Abdominal pain related to stool consistency	.20	.07	.11	<u>.85</u>	.08	.19	.05	.04
43	Abdominal pain related to stool frequency	.22	.08	.16	<u>.75</u>	.13	.23	.10	.03
45	Abdominal pain related to a meal	.09	.13	.33	.38	.13	.25	.22	.04
46	Abdominal pain limits usual activities	.17	.14	<u>.54</u>	.27	.24	.16	.10	.05
49	Hard stools	<u>.61</u>	.13	.10	.14	.08	-.03	.12	.07
51	Infrequent stools	<u>.55</u>	.08	.18	.08	.14	.03	.04	.06
52	Straining during bowel movements	<u>.80</u>	.16	.09	.18	.08	.04	.11	.06
53	Incomplete bowel emptying	<u>.72</u>	.19	.13	.20	.12	.20	.09	.06
54	Anorectal obstruction / blockage	<u>.81</u>	.20	.14	.14	.10	.10	.09	.06
55	Manual manoeuvres to facilitate defecation	<u>.52</u>	.14	.13	.05	.11	.04	.10	-.01
59	Loose stools	.07	.21	.09	.21	.15	<u>.73</u>	.08	.03
61	Loose stools following a meal	.03	.05	.17	.21	.09	<u>.64</u>	.11	.06
63	Urgency	.20	.25	.18	.20	.12	<u>.64</u>	.10	.03
65	Bloating / abdominal distension	.37	<u>.42</u>	.20	.15	.03	.27	.07	.08
68	Right upper quadrant pain	.25	<u>.63</u>	.38	.09	.14	.17	.01	.03
69	Long-lasting right upper quadrant pain	.18	.18	<u>.71</u>	.08	.12	.09	.10	.07
70	Right upper quadrant pain of steady severe level	.19	.17	<u>.74</u>	.09	.14	.14	.07	.05
71	Right upper quadrant pain at different intervals	-.07	-.12	-.12	.11	-.10	.01	.03	-.02
72	Right upper quadrant pain limits usual activities	.12	.19	<u>.63</u>	.07	.26	.07	.07	.04
73	Right upper quadrant pain related to defecation	.17	.07	.13	<u>.48</u>	.05	.14	.01	.03
74	Right upper quadrant pain related to posture	.10	.02	.08	.13	.09	.06	.15	.00
75	Right upper quadrant pain improved by medicine	.05	.08	.04	.01	.05	.05	<u>.42</u>	-.01
76	Right upper quadrant pain related to vomiting	.11	.16	.37	.05	<u>.57</u>	.10	.17	.04
77	Right upper quadrant pain related to back pain	.18	.21	<u>.40</u>	.07	.14	.07	.17	.05
78	Right upper quadrant pain waking one up	.13	.25	<u>.51</u>	.04	.26	.15	.15	.00
80	Faecal incontinence	.11	.28	.07	.09	.13	.36	.05	.01
83	Anorectal pain	.38	.38	.13	.12	.11	.17	.02	.04







Supplementary material

This supporting document presents exploratory factor analysis results separate for the three countries. Methods are identical to those described in the main text.

Results are presented in supplementary tables 1-3. Briefly, factors were highly similar across the individual countries. There emerged factors for IBS, constipation, diarrhoea, abdominal pain, nausea and/or vomiting, and upper GI symptoms in all models. Heartburn and globus were part of the upper GI symptom factor in the US sample.

Supplementary table 1: Factor loadings in US sample after varimax rotation.

Item	Topic	Upper GI	Abdominal pain	Constipation	Upper GI II	Nausea/vomiting	IBS	Diarrhoea
1	Lump in throat	<u>.54</u>	.11	.19	.17	.11	.00	.08
3	Lump in throat when not eating	.33	.20	.14	<u>.49</u>	.10	.07	-.02
4	Pain with swallowing	.34	.33	.15	.27	.20	.07	.02
5	Chest pain	<u>.59</u>	.21	.22	.05	.13	.01	.12
7	Chest pain as burning sensation	<u>.49</u>	.17	.12	.28	.07	.22	.06
8	Chest pain and food sticking after swallowing	<u>.40</u>	.08	.11	.39	.18	.17	.00
9	Heartburn	<u>.61</u>	.09	.15	.12	.08	.13	.11
12	Foods stuck in chest	<u>.63</u>	.14	.16	.19	.16	.04	.10
14	Postprandial fullness	<u>.46</u>	.26	.22	.05	.23	-.02	.16
16	Early satiety	<u>.40</u>	.24	.27	.02	.28	.04	.17
18	Epigastric pain/burning	<u>.60</u>	.37	.17	.02	.24	.03	.13
19	Epigastric pain/burning improved by defecation	.08	.01	.13	<u>.59</u>	-.04	.37	.03
21	Nausea	<u>.42</u>	.31	.21	.03	<u>.58</u>	.08	.15
23	Vomiting	<u>.42</u>	.18	.13	.07	<u>.66</u>	.05	.08
25	Self-induced vomiting	.20	.05	.10	<u>.54</u>	.26	.02	.04
32	Food coming back up after swallowing	<u>.59</u>	.11	.14	.17	.33	.09	.14
34	Retching	.30	.24	.12	.33	<u>.55</u>	.12	.16
35	Vomiting when food comes back up	.22	.33	.21	.11	<u>.62</u>	.17	.10
37	Food coming back up is recognisable	.13	.19	.05	<u>.50</u>	.24	.11	.01
38	Belching	<u>.49</u>	.19	.13	.22	.25	.01	.12
40	Pain anywhere in the abdomen	<u>.56</u>	<u>.44</u>	.26	-.10	.13	.12	.20
41	Abdominal pain related to defecation	.02	.04	.18	.33	.00	<u>.68</u>	.16
42	Abdominal pain related to stool consistency	.08	.09	.23	.16	.11	<u>.85</u>	.15
43	Abdominal pain related to stool frequency	.13	.19	.25	.14	.12	<u>.74</u>	.20
45	Abdominal pain related to a meal	.25	.35	.15	.21	.14	.36	.22
46	Abdominal pain limits usual activities	.14	<u>.59</u>	.23	.00	.28	.24	.19
49	Hard stools	.21	.15	<u>.56</u>	.14	.11	.12	-.06
51	Infrequent stools	.13	.17	<u>.55</u>	.12	.12	.12	.04
52	Straining during bowel movements	.22	.09	<u>.80</u>	.09	.05	.23	.07
53	Incomplete bowel emptying	.25	.14	<u>.72</u>	.05	.11	.24	.21
54	Anorectal obstruction / blockage	.23	.20	<u>.79</u>	.07	.12	.14	.11
55	Manual manoeuvres to facilitate defecation	.20	.23	<u>.46</u>	.22	.15	.02	.02
59	Loose stools	.29	.08	.08	.10	.15	.23	<u>.75</u>
61	Loose stools following a meal	.16	.20	.03	.22	.11	.20	<u>.64</u>
63	Urgency	.32	.19	.22	.15	.10	.18	<u>.62</u>
65	Bloating / abdominal distension	.39	.25	<u>.41</u>	-.03	.04	.14	.29
68	Right upper quadrant pain	<u>.55</u>	<u>.49</u>	.24	-.11	.15	.14	.20
69	Long-lasting right upper quadrant pain	.28	<u>.67</u>	.24	.03	.12	.10	.08
70	Right upper quadrant pain of steady severe level	.23	<u>.69</u>	.24	.10	.13	.10	.15
71	Right upper quadrant pain at different intervals	-.09	-.09	-.06	.32	-.06	.04	.08
72	Right upper quadrant pain limits usual activities	.17	<u>.68</u>	.12	.10	.26	.06	.03
73	Right upper quadrant pain related to defecation	.05	.14	.24	<u>.42</u>	.06	.33	.18
74	Right upper quadrant pain related to posture	.06	.08	.08	.29	.06	.06	.09
75	Right upper quadrant pain improved by medicine	.25	.05	.07	.36	-.01	.06	.06
76	Right upper quadrant pain related to vomiting	.30	.36	.14	.25	<u>.59</u>	.04	.11
77	Right upper quadrant pain related to back pain	.31	<u>.44</u>	.20	.28	.08	.02	.03
78	Right upper quadrant pain waking one up	.33	<u>.51</u>	.10	.20	.20	.05	.14
80	Faecal incontinence	.38	.10	.13	.19	.15	.09	.30
83	Anorectal pain	<u>.40</u>	.17	.36	.17	.19	.12	.15

Supplementary table 2: Factor loadings in Canadian sample after varimax rotation.

Item	Topic	Upper GI	Abdominal pain	Constipation	IBS	Diarrhoea	Nausea/vomiting	Globus
1	Lump in throat	<u>.41</u>	-.03	.13	.04	.06	.07	<u>.43</u>
3	Lump in throat when not eating	.05	.09	.07	.15	.10	.03	<u>.64</u>
4	Pain with swallowing	.20	.12	.09	.12	.03	.05	.11
5	Chest pain	<u>.54</u>	.06	.17	-.02	.07	.09	.21
7	Chest pain as burning sensation	.11	.18	.07	.06	.06	.02	.16
8	Chest pain and food sticking after swallowing	.21	.00	.08	.11	.00	.08	-.08
9	Heartburn	<u>.49</u>	.10	.14	.05	.11	.02	.05
12	Foods stuck in chest	<u>.54</u>	.01	.16	.04	.11	.06	.04
14	Postprandial fullness	<u>.56</u>	.16	.14	.03	.11	.04	-.06
16	Early satiety	<u>.53</u>	.10	.17	.06	.12	.11	-.02
18	Epigastric pain/burning	<u>.58</u>	.34	.14	.05	.07	.03	.04
19	Epigastric pain/burning improved by defecation	.01	-.12	.12	<u>.43</u>	-.01	.06	.17
21	Nausea	<u>.50</u>	.34	.11	.08	.10	.32	.07
23	Vomiting	.33	.26	.10	.04	.04	<u>.48</u>	.06
25	Self-induced vomiting	-.08	.05	.02	-.09	.02	.08	.11
32	Food coming back up after swallowing	<u>.53</u>	.08	.17	.09	.10	.26	.09
34	Retching	.21	.09	.07	.04	.03	<u>.49</u>	.11
35	Vomiting when food comes back up	.17	.16	.18	.02	.14	<u>.76</u>	-.05
37	Food coming back up is recognisable	.12	.01	.01	.06	-.02	.05	.12
38	Belching	<u>.46</u>	.10	.07	.03	.06	.09	-.05
40	Pain anywhere in the abdomen	<u>.52</u>	<u>.41</u>	.24	.07	.19	.03	.15
41	Abdominal pain related to defecation	.01	.09	.14	<u>.73</u>	.16	.02	.08
42	Abdominal pain related to stool consistency	.10	.17	.19	<u>.88</u>	.19	.02	.11
43	Abdominal pain related to stool frequency	.13	.22	.21	<u>.66</u>	.25	.04	.02
45	Abdominal pain related to a meal	.18	.34	.09	.30	.28	-.05	.08
46	Abdominal pain limits usual activities	.23	<u>.53</u>	.18	.17	.17	.10	.05
49	Hard stools	.18	.06	<u>.64</u>	.12	.00	-.03	.09
51	Infrequent stools	.08	.21	<u>.53</u>	.01	.04	.14	.09
52	Straining during bowel movements	.21	.11	<u>.80</u>	.12	.04	.05	.10
53	Incomplete bowel emptying	.22	.22	<u>.71</u>	.16	.17	.11	.02
54	Anorectal obstruction / blockage	.23	.12	<u>.82</u>	.12	.09	.08	.05
55	Manual manoeuvres to facilitate defecation	.11	.14	<u>.56</u>	.07	.01	.04	-.10
59	Loose stools	.19	.15	.04	.12	<u>.74</u>	.08	.07
61	Loose stools following a meal	.06	.11	.00	.16	<u>.66</u>	.00	.14
63	Urgency	.23	.20	.18	.14	<u>.68</u>	.09	-.02
65	Bloating / abdominal distension	.39	.20	.34	.14	.33	-.03	-.03
68	Right upper quadrant pain	<u>.48</u>	<u>.40</u>	.26	.05	.19	.04	.11
69	Long-lasting right upper quadrant pain	.06	<u>.71</u>	.15	.09	.14	.04	.10
70	Right upper quadrant pain of steady severe level	.12	<u>.75</u>	.17	.13	.17	.01	.02
71	Right upper quadrant pain at different intervals	-.12	-.14	-.08	.07	-.02	-.05	.02
72	Right upper quadrant pain limits usual activities	.14	<u>.69</u>	.13	.09	.08	.13	.04
73	Right upper quadrant pain related to defecation	.06	.14	.16	<u>.58</u>	.16	.06	.02
74	Right upper quadrant pain related to posture	.12	.07	-.01	.10	.01	.08	-.03
75	Right upper quadrant pain improved by medicine	.15	.06	.05	.02	.02	.07	-.06
76	Right upper quadrant pain related to vomiting	.16	<u>.49</u>	.05	.04	.05	<u>.42</u>	.06
77	Right upper quadrant pain related to back pain	.20	<u>.46</u>	.17	.06	.07	.09	-.04
78	Right upper quadrant pain waking one up	.16	<u>.58</u>	.16	.05	.09	.15	-.03
80	Faecal incontinence	.16	.10	.09	.14	.36	.10	-.03
83	Anorectal pain	.26	.15	.37	.13	.20	.05	.00

Supplementary table 3: Factor loadings in UK sample after varimax rotation.

Item	Topic	Constipation	Upper GI	Abdominal pain	IBS	Diarrhoea	Vomiting	Nausea	Heartburn	Abdominal pain II
1	Lump in throat	.18	<u>.56</u>	.03	.01	.10	-.04	-.02	.02	.02
3	Lump in throat when not eating	.08	.14	.12	.07	.00	.03	.02	.11	.01
4	Pain with swallowing	.08	.35	.14	.05	.03	.18	.09	.20	.03
5	Chest pain	.21	<u>.49</u>	.05	-.04	.09	.14	.06	.07	.16
7	Chest pain as burning sensation	.03	.11	.15	.10	.03	.00	.00	<u>.97</u>	.01
8	Chest pain and food sticking after swallowing	.02	<u>.44</u>	.11	.17	.05	.05	.00	.27	-.16
9	Heartburn	.19	<u>.40</u>	.02	-.01	.14	.04	.07	<u>.42</u>	.15
12	Foods stuck in chest	.20	<u>.68</u>	.00	.05	.10	.05	.02	.11	.00
14	Postprandial fullness	.17	<u>.52</u>	.20	.08	.12	.18	.10	.02	.09
16	Early satiety	.20	<u>.42</u>	.22	.03	.13	.20	.13	.03	.07
18	Epigastric pain/burning	.15	<u>.57</u>	.22	.04	.10	.06	.22	.12	.26
19	Epigastric pain/burning improved by defecation	.11	.07	-.04	<u>.44</u>	-.01	.07	.05	.22	-.04
21	Nausea	.18	<u>.40</u>	.26	.02	.12	.19	<u>.51</u>	.01	.16
23	Vomiting	.10	.31	.11	.10	.08	<u>.40</u>	.39	.01	.10
25	Self-induced vomiting	.03	.03	-.10	.09	.09	.10	-.05	.07	.03
32	Food coming back up after swallowing	.16	<u>.45</u>	.04	.10	.13	.22	.25	.07	.08
34	Retching	.15	.19	.13	.10	.12	<u>.68</u>	.09	-.01	.00
35	Vomiting when food comes back up	.13	.19	.17	.07	.14	<u>.79</u>	.15	-.02	.06
37	Food coming back up is recognisable	.04	.10	.09	.13	.00	.13	.09	.01	.04
38	Belching	.07	<u>.40</u>	.20	.07	.15	.08	.30	.02	.11
40	Pain anywhere in the abdomen	.28	.29	.23	.09	.24	.09	.03	.01	<u>.68</u>
41	Abdominal pain related to defecation	.12	-.01	.05	<u>.75</u>	.11	.02	-.04	-.03	.03
42	Abdominal pain related to stool consistency	.20	.07	.07	<u>.80</u>	.25	.05	-.03	-.01	.09
43	Abdominal pain related to stool frequency	.23	.08	.08	<u>.73</u>	.29	.09	.06	.03	.08
45	Abdominal pain related to a meal	.04	.16	.32	.36	.27	.13	.14	.08	.07
46	Abdominal pain limits usual activities	.11	.17	<u>.54</u>	.29	.17	.10	.21	.05	.12
49	Hard stools	<u>.66</u>	.11	.10	.14	-.02	.06	.05	.06	.02
51	Infrequent stools	<u>.57</u>	.10	.11	.08	-.01	.14	.05	-.01	.07
52	Straining during bowel movements	<u>.82</u>	.13	.08	.14	.01	.07	.06	.04	.09
53	Incomplete bowel emptying	<u>.73</u>	.09	.06	.14	.24	.10	.04	.08	.14
54	Anorectal obstruction / blockage	<u>.83</u>	.17	.13	.14	.14	.06	.03	.04	.07
55	Manual manoeuvres to facilitate defecation	<u>.56</u>	.17	.02	.05	.11	.00	.06	-.01	-.04
59	Loose stools	.10	.13	.07	.22	<u>.70</u>	.14	.02	.03	.11
61	Loose stools following a meal	.07	.08	.15	.22	<u>.64</u>	.04	.01	.06	-.04
63	Urgency	.19	.18	.16	.26	<u>.62</u>	.12	.08	-.01	.09
65	Bloating / abdominal distension	.39	.27	.19	.08	.27	-.08	.10	.05	.33
68	Right upper quadrant pain	.28	.32	.30	.07	.21	.11	.07	.07	<u>.53</u>
69	Long-lasting right upper quadrant pain	.15	.11	<u>.74</u>	.02	.02	.04	.08	.08	.14
70	Right upper quadrant pain of steady severe level	.15	.11	<u>.83</u>	.02	.12	.13	.05	.05	.00
71	Right upper quadrant pain at different intervals	-.06	-.21	-.16	.16	-.04	-.13	.03	-.01	-.02
72	Right upper quadrant pain limits usual activities	.11	.30	<u>.58</u>	.03	.14	.06	.29	-.04	.00
73	Right upper quadrant pain related to defecation	.15	.00	.08	<u>.54</u>	.13	.01	.08	-.05	-.02
74	Right upper quadrant pain related to posture	.22	.05	.08	.17	.06	-.02	.23	.08	-.10
75	Right upper quadrant pain improved by medicine	.02	.18	.01	-.05	.02	-.06	.10	.25	.00
76	Right upper quadrant pain related to vomiting	.14	.17	.27	.00	.11	.21	<u>.62</u>	.11	.00
77	Right upper quadrant pain related to back pain	.15	.23	.19	.10	.08	.09	.13	.02	.02
78	Right upper quadrant pain waking one up	.12	.26	.39	.04	.22	.15	.29	.00	.14
80	Faecal incontinence	.12	.15	-.02	.03	<u>.44</u>	.02	.15	.03	.14
83	Anorectal pain	<u>.42</u>	.24	.08	.09	.22	.00	.10	-.02	.21